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ARAŞTIRMA / RESEARCH

Comparison of efficacy of intraarticular polyacrylamide hydrogel and methylprednisolone acetate in patients with knee osteoarthritis

Diz osteoartriti olan hastalarda eklem içi poliakrilamid hidrojel ve metilprednizolon asetatın etkinliğinin karşılaştırılması

Ahmet Issın[1], Nizamettin Koçkara[1], İsmet Yalkın Çamurcu[1]

[1]Erzincan Üniversitesi Tıp Fakültesi, Ortopedi ve Travmatoloji Anabilim Dalı, Erzincan, Turkey

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Abstract

Purpose: The aim of this study was to compare and evaluate the efficacy of intraarticular methylprednisolone acetate and an intra-articular polyacrylamide hydrogel in patients with different stages of knee osteoarthritis.

Materials and Methods: Patients with symptomatic knee osteoarthritis and history of failed pharmacotherapy or physiotherapy interventions were included in this study. The first 64 consecutive patients got intra-articular polyacrylamide hydrogel, the latter 79 consecutive patients got intra-articular methylprednisolone acetate. Patients were evaluated by WOMAC score and self-assessment questions.

Results: There was no statistically significance difference between groups when WOMAC scores and answers of self-assessment questions were compared.

Conclusion: Intra-articular use of polyacrylamide hydrogel was not superior to methylprednisolone acetate, for patients with knee osteoarthritis.

Key words: osteoarthritis, gonarthrosis, methylprednisolone acetate, injection.

Öz

Amaç: Bu çalışmanın amacı, farklı evrelerde diz osteoartriti olan hastalarda eklem içi metilprednizolon asetat ve eklem içi poliakrilamid hidrojelin etkinliğini karşılaştırmak ve değerlendirmektir.

Gereç ve Yöntem: Semptomatik diz osteoartriti olan ilaç veya fizik tedaviden fayda görmemiş hastalar çalışmaya dahil edildi. İlk 64 hasta eklem içi poliakrilamid hidrojel tedavisi aldı, sonraki 79 hasta ise eklem içi metilprednizolon asetat tedavisi aldı. Hastalar WOMAC skoru ve özdeğerlendirme soruları ile değerlendirildi.

Bulgular: WOMAC skorları ve özdeğerlendirme sorularının cevapları karşılaştırıldığında gruplar arasında istatistiksel olarak anlamlı bir fark yoktu.

Sonuç: Diz osteoartriti olan hastalarda, eklem içi poliakrilamid hidrojelin kullanımı metilprednizolon asetata göre üstün değildir.

Anahtar kelimeler: Osteoartrit, gonartroz, metilprednizolon asetat, enjeksiyon.

INTRODUCTION

Knee osteoarthritis is the most common degenerative joint disease, which is characterized by pain and dysfunction[1]. Pain relief and therefore increased function are the main goals of the treatment. Intra-articular corticosteroid injections are widely used in the literature and authors reported successful results[2-4]. Among the most common types of intra-articular corticosteroids, methylprednisolone acetate (MP) has a long lasting effect and it was recommended in the relevant studies[5,6].

Polyacrylamide hydrogels (PHG) are biocompatible, synthetic polymers that are being used as an augmentation material in cosmetic and soft tissue surgeries[7,8]. PHG is a biocompatible, bio-stable material and its viscosity is adequate for injection. Intra-articular use of them was proposed and became popular in Russia and Asian countries. They were claimed to be effective for the symptomatic treatment of knee osteoarthritis. Previously, Zan and Bodugoz et al investigated the efficacy of IA PHG for symptomatic knee OA[9-10]. "Turkish Ministry of

Yazışma Adresi/Address for Correspondence: Dr. Ahmet Issın, Erzincan Üniversitesi Tıp Fakültesi, Ortopedi ve Travmatoloji Anabilim Dalı, Erzincan, Turkey. E-mail: Ahmet.issin@gmail.com
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Health" approved its use and the cost had been funded by the national public health insurance.

The aim of this study was to compare and evaluate the efficacy of intra-articular MP and PHG in patients with different stages of knee osteoarthritis.

MATERIALS AND METHODS

This single-center, quasi-randomized and prospective clinical study was conducted in Erzincan University Faculty of Medicine, Department of Orthopaedics and Traumatology according to Helsinki Declaration under approval of institutional ethical committee. Patients, who were admitted to our clinic between the dates 01.10.2014 and 01.06.2015 with symptomatic primary knee osteoarthritis, with the radiologic signs as well as history of failed pharmacotherapy/physiotherapy interventions were included in the study. Patients with the history of; previous intra-articular injection, surgical intervention on the affected knee, rheumatologic diseases and the patients who had only patella-femoral pain were excluded from the study. Anterior-posterior, lateral knee and tangential patella radiographs were taken for all the patients. Radiographs were staged according to Kellgren-Lawrence classification.

A single dose intra-articular 2.5mL PHG (Noltrex, Bioform, Moscow, Russia) injection was performed for the first 64 consecutive patients. Intra-articular single-dose 1mL/40mg MP (Depo-Medrol, Eczacibasi, Istanbul, Turkey) injection was performed for the latter 79 consecutive patients. By the help of a physician, all patients were required to fill Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) and WOMAC pain subscale prior to intra-articular injection and at 12th week follow-up.

Informed consent was obtained for all patients before the intra-articular injection procedure. All injections were performed in the same manner by one of the attending physician involved in the study. The patient was placed in sitting position with knee flexed at 90 degrees. Skin was prepared with alcohol and the needle was inserted from anteromedial knee portal to the joint space. Intra-articular PHG was given with the use of manufacturer's prefilled syringe and MP was given after mixing with 4mL of prilocaine (10mL 2% Citanest, Eczacibasi, Kirklareli, Turkey) before the injection.

At 12th week follow-up, some basic questions were asked to all the patients for determining the self-assessment of their clinical status and satisfaction level. Questions were kept simple regarding to the socio-cultural characteristics of the patients yet they provided enough data for statistical evaluation.

These questions were:

1) Did the intra-articular injection ever decreased your pain? (binary)
2) How long the intra-articular injection decreased your pain? (1,3,6,9,12 weeks)
3) How is the pain now compared to before? (worse, same, low, much lower)
4) How much pain did you feel during the injection? (low, much)
5) How much did you satisfy by intra-articular injection? (low, medium, high)
6) Would you like to try this injection again or recommend it to someone else? (binary)

Statistical analysis

Statistical analysis was performed to ascertain the effects of two treatments by using SPSS 22.0 software (SPSS Inc., IBM, Chicago, IL, USA). Continuous variables were given as means and standard deviation, categorical variables were given as frequencies and percentages. Z-test was used to determine the significance of the difference between two percentages; T-test was used for continuous variables such as the pain scores.

RESULTS

The demographic data of the patients and stages of knee osteoarthritis according to Kellgren-Lawrence classification were shown in Table 1. Before the intra-articular injection, the mean WOMAC scores were 69.9 ± 9.1 points (ranges, 64 to 84 points) in PHG group and 62.6 ± 11.7 points (ranges, 41 to 80 points) in the MP group. The mean WOMAC pain subscale scores were 11.5 ± 3.5 points (ranges, 5 to 18 points) and 9.8 ± 3.6 points (ranges, 4 to 18 points) for PHG and MP groups respectively before the intra-articular injection. The difference between the groups was not statistically significant ($p>0.05$).

At 12th week control, these scores were 10.5 ± 4 points (ranges, 5 to 18 points) and 8.6 ±3.4 points

(ranges, 4 to 16 points). The average change in pain score in PHG group was 1 ±1.8 points (ranges, -2 to 5) and 1.2 ±1.8 points (ranges, -1 to 7) in MP group. There was not a statistically significant difference (p>0.05) (Table 2). In the PHG group, 54.7% of the patients reported that they had some benefit from the injection, while that ratio was 64.6% for MP group. There was no significant difference between the groups (p>0.05). The self-assessment questions and the answers of the patients were listed in Table 3.

Table 1 Demographic data and Kellgren-Lawrence classifications of the patients.

	Polyacrylamide hydrogel group (n=64)	**Methylprednisolone acetate group (n=79)**
Gender (female/male)	46 / 18	54 / 25
Age*	62.3 ± 9.7 (40 - 78)	65.7 ± 8.8 (50 - 86)
Kellgren-Lawrence Classification		
Stage 1	13 patients	5 patients
Stage 2	20 patients	15 patients
Stage 3	25 patients	48 patients
Stage 4	6 patients	11 patients

* Mean ± standart deviation (range)

Table 2 Comparison of WOMAC scores of the patients

	PHG group (n=64)	**MP group (n=79)**	**P**
WOMAC			
Before injection	70 ± 9.1 (64-84)	63 ± 11.7 (41-80)	>0.05
12th week	74 ± 11.2 (64-89)	67 ± 10.1 (46-84)	>0.05
WOMAC Pain Subscale			
Before injection	12 ± 3.5 (5-18)	10 ± 3.6 (4-18)	>0.05
12th week	11 ± 4 (5-18)	9 ±3.4 (4-16)	>0.05

* Mean ± standart deviation (range)

Table 3 Self-assessment questions and answers of the patients with p values

Self-assessment question	**PHG group**		**MP group**		***P****
	Answer	**% of patients**	**Answer**	**% of patients**	
1) Did the intra-articular injection ever decreased your pain?	yes	55%	yes	5%	>0.05
	no	45 %	no	35 %	>0.05
2) How long the intra-articular injection decreased your pain?	1 week	none	1 week	5%	>0.05
	3 week	14%	3 week	18%	>0.05
	6 week	23%	6 week	37%	>0.05
	9 week	34%	9 week	24%	>0.05
	12 week	29%	12 week	16%	>0.05
3) How is the pain now compared to before?	worse	25%	worse	7%	**<0.05**
	same	16%	same	27%	>0.05
	low	31%	low	33%	>0.05
	much lower	28%	much lower	33%	>0.05
4) How much pain did you feel during the injection?	low	74%	low	96%	>0.05
	much	26%	much	5%	>0.05
5) How much did you satisfy by intra-articular injection?	low	37%	low	37%	>0.05
	medium	43%	medium	39%	>0.05
	high	20%	high	24%	>0.05
6) Would you like to try this injection again or recommend it to someone else?	yes	48%	yes	63%	>0.05
	no	52%	no	37%	>0.05

* p values after z test

There were also no significant differences between the groups in patient satisfaction when patients were grouped according to their age (<65 years old, >65 years old) and their WOMAC score (<65 points, > 65 points). Within PHG group, patients with Kellgren-Lawrence type 2 and 3 knees had better pain reduction then type 1 and 4 after intra-articular injection ($p<0.05$). However, there was no significant difference within MP group when patients were grouped by Kellgren-Lawrence classification ($p>0.05$). The self-assessment questions and the answers of the patients were listed in Table 3 with the p values.

DISCUSSION

Osteoarthritis of knee joint is a slowly progressing disease, however there is not effective remedy that reduces or reverses the degenerative changes that occurred to the cartilaginous tissue. Symptomatic treatment aims to reduce the pain, increase the range of motion and maintain a desired quality of life. For these purposes; non-steroidal anti-inflammatory drugs, physical therapy modalities and braces are the most common used conservative treatment methods[11,12]. Intra-articular injections are recommended as an alternative in the conservative management when other methods were not efficient. While choosing the appropriate intra-articular agent, some situations should be considered. If the goal of the treatment is to decrease pain, local anesthetics are perfect in short-term pain relief. However, intra-articular injection of corticosteroids was reported to reduce the inflammation and pain for a relatively longer period of time[2-4]. By symptomatic relief in knee osteoarthritis, MP was shown to be the most effective one among the corticosteroids [5]. Joint lavage and sham injections were also shown to reduce the pain up to weeks, which may be explained by the placebo effect[13-15].

This study evaluated the clinical results of intra-articular MP and PHG injection, by comparing the pain scores and patient self-assessment questionnaires. In such studies, pain perception is a highly subjective variable and pain relief by placebo is highly dependent on the expectations of the patients[12]. Therefore, the analgesic effect of placebo, especially when used intraarticular, is strong in osteoarthritis[13].

Polyacrylamide-hydrogels are claimed to be effective for the symptomatic treatment of knee osteoarthritis. A few studies were found about the intra-articular use of PHG in the literature[9,10]. PHG is a biocompatible, bio-stable material and its viscosity is adequate for injection. However, gel form lacks the strength and toughness to serve as a cartilage substitute material and thus force dampening effect is negligible[10]. They may reduce the friction within the surfaces for some and that mechanical benefit may reduce the pain in selected circumstances, however such a benefit in knee osteoarthritis was limited.

In our study, 54.7% of the patients in the PHG group and 64.6% of the patients in the MP group reported that they had benefit from the injection. However, the difference was not statistically significant. Despite the biocompatibility of PHG, serious foreign body reaction was reported in the literature [16]. In this study, we did not perform PHG injection in patients with the presence of synovitis or effusion; however, 25% of the patients in PHG group complained about pain at 12th week control. This ratio was 7.6% in MP group and the difference between the groups was statistically significant ($p<0.05$). We observed that, intra-articular injection of PHG was more painful than MP injection. This can be explained by lack of anesthetic substance in PHG syringes or maybe this discomfort is due to a subtle foreign-body reaction. The main limitation of this study was, patient groups were not homogeneous to compare clinical results. However, this study stated important findings in a relatively large patient population with clinical scores and self-assessment questions. The main important finding of this study was that; intra-articular use of polyacrylamide hydrogel, is an expensive and non-beneficial treatment alternative in knee osteoarthritis, when compared to corticosteroid. In addition to that, the presence of discomfort after PHG injection is another important consideration for the choice of intra-articular agent.

In conclusion, intra-articular use of polyacrylamide hydrogel was not superior to methylprednisolone acetate in short-term pain reduction and patient satisfaction for the patients with the diagnosis of knee osteoarthritis.

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